PROFILES

Rebecca Saxe: Fine tuning the theory of mind

BY **VIRGINIA HUGHES**

26 JANUARY 2009

One day last November, as she does several times a week, cognitive scientist **Rebecca Saxe** gave a lecture about the brain. This time, her audience was not other scientists or philosophers or undergraduates at the Massachusetts Institute of Technology (MIT), but the 80-odd honorable members of the Rhode Island judiciary.

Saxe packed her talk with "super-cool things about the brain," she recalls. She told the judges how the brain folds precisely the same way in every human; and how most of the stuff inside of our brains is not the brain cells, called gray matter, but the connections between the cells, or white matter.

Saxe, 29, is not much taller than 5 feet. Exceedingly unpretentious and usually shy, she becomes quite animated when she delves into the mysteries of the human brain. Alas, the judges did not share her enthusiasm. "Their reaction was, 'Mmm, that's nice,'" she recalls with a laugh. "I just totally miscalled it."

The incident is rendered ironic by Saxe?s research focus: the ability to divine what others are thinking.

This ability to sense what other people want, believe or intend is called the '**theory of mind**.' The idea has fascinated philosophers and psychologists for centuries, but it wasn't until 2003 that Saxe, then a 24-year-old graduate student, identified a precise region in the brain ? the temporo-parietal junction, or TPJ ? that's preferentially active when we think about what others are thinking[1].

"It was a truly remarkable discovery," says **Nancy Kanwisher**, a cognitive neuroscientist at MIT, and Saxe's Ph.D. advisor. "The very part of the brain that she's made this major discovery on is the one that seems most likely to play a major role in autism."

In the past year, now working in her own lab in MIT's Brain and Cognitive Sciences department, Saxe has been designing brain-imaging experiments to study infant brain development, moral judgment and theory of mind in people with autism, who often have trouble grasping others? thoughts.

For instance, in experiments beginning this month, she is using a new procedure that uses live video to observe brain activity during real-time, back-and-forth social interaction ? a measure that she predicts will be strikingly different in people with autism.

The common thread in all of Saxe's research, including her recent foray into autism, is discovering what makes the human brain unique among animals.

"There might be reason to believe that our high-level social capacities just are different than any other animal. And to the extent that that's true, we need to study the neural basis of human beings, because that's the only place they are," she says.

Early success:

Saxe has been fascinated with humanness since, as a young girl, she learned that humans are made up of tiny atoms. "I thought that was the most astonishing thing I had ever heard," she says. "That you could put together a whole person out of pieces, it was just totally mind-boggling; it remains totally mind-boggling."

Because DNA is the smallest of those biological pieces, her curiosity led her to first consider studying genetics. But that didn't last long. Genes build the body ? and she wanted to unlock the mind. "That story is not told entirely in the genes. In fact, it's probably not told mostly in the genes," she says. By the end of high school, she had decided to become a cognitive scientist.

In the fall of 1997, Saxe moved from Toronto, Canada, to the University of Oxford in England. There, she studied attention in renowned cognitive scientist **Kia Nobre's lab**, and graduated with a Congratulatory First honors distinction.

Turning to more social aspects of the mind, Saxe next moved to the sleek McGovern Institute for Brain Research at MIT, where she began her Ph.D.

"When she walked in the door for her interview, it was obvious within five minutes that she had a totally superior intellect," Kanwisher says. "I knew I wanted her in my lab right away."

Saxe's Ph.D. thesis, completed in 2003, resulted in several major findings, the most celebrated of which was pinpointing the temporo-parietal junction as the brain's Theory of Mind nexus. It won an

Outstanding Thesis Award from MIT's Brain and Cognitive Sciences department, and was eventually published in four peer-reviewed papers[2,3,4].

That same year, she was accepted as a junior fellow into Harvard University's **Society of Fellows**, an elite program that grants scholars three years of financial support to use however they wish. For the following three years, while conducting research in Harvard professor **Susan Carey**'s developmental psychology lab, Saxe happily fulfilled the program's only significant requirement: joining the other fellows for Monday dinners, Tuesday lunches and Friday lunches.

The Monday dinners were lavish, five-course affairs, held in a wood-paneled dining room. They always included a chocolate course, which Saxe once used for an experiment on those sitting at her table.

She gave her tablemates chocolates from different regions of the world, each with different proportions of cocoa and butter, then asked them to describe how they tasted and to guess which ones were which.

"It's illustrative of Rebecca's personality: using the scientific method, in a fairly rigorous manner, both to give pleasure and to try to investigate the nuances of human experience," recalls **Elisabeth Camp**, assistant professor of philosophy at the University of Pennsylvania, who participated in the impromptu experiment and remains one of Saxe's close friends.

Part of that human experience is philosophy, language and literature, subjects about which Saxe is constantly trying to learn more.

In February 2007, Camp, Saxe and **Vanessa Ryan**, another junior fellow, went to Rutgers University in New Jersey to give a talk contrasting how the theory of mind is used in philosophy, literature and cognitive science.

On the plane ride, Saxe abruptly asked Ryan to explain how she taught literature. "She pulled out the *London Review of Books* or something, pointed to a poem that I'd never read and she'd never read, and said, 'Let's do a class'," recalls Ryan, an assistant professor of English at Brown University. "Rebecca has a real curiosity and willingness to engage in what she doesn't know," she adds.

Saxe describes the Society of Fellows as a "quite awesome social-intellectual world" that was full of "quite interesting people" ? one of whom, **Allan Adams**, a glider pilot and an assistant professor of physics at MIT, she married in September 2007.

Live feeds:

One Tuesday afternoon in early December, Saxe stood at the back of the dim technician's room for

MIT's human functional magnetic resonance imaging (fMRI) machine, watching intently as one of her postdoctoral fellows scanned the brain of a female college student. Gray and white images of the woman's brain popped up on one of the computers. "Have you ever seen a brain before?" Saxe whispered excitedly.

So far, Saxe has used fMRI to measure the brain regions involved not only in the Theory of Mind, but in making personality judgments[5], moral judgments[6], and even listening to action verbs[7].

In a typical fMRI experiment, the participant lies confined in a coffin-like machine that measures magnetic changes in blood flow across the brain. Because active neurons use more blood than inactive neurons, this picture gives scientists an approximation of which brain regions are more active than others during specific tasks, such as listening to a word or making a moral decision about a hypothetical situation.

The participant must keep as still as possible, however, which makes measuring brain activity during real-time social interaction impossible, or nearly so.

In the past couple of months, Saxe has designed a new paradigm that gets around this hurdle. In the set up, the participant watches, through an angled mirror, video footage projected onto a screen behind the fMRI machine, and is himself videotaped while watching it. This creates a live feed in which the participant and an experimenter sitting in another room can interact with each other in real time.

For instance, in one experiment, the researcher shows the participant two buckets, each with a toy hidden inside, and asks the participant to look at the bucket in which they'd like to see the toy. While this goes on, the fMRI machine records how his brain is responding to various parts of the interaction.

In a subsequent trial, the participant is shown the video footage of the previous interaction, rather than a live feed.

Previous experiments have shown that infants as young as 3 months of age can detect when a live video of a social interaction with their mother has been swapped for a taped one. "Babies react very negatively to that, they cry. Even though what their mom is doing is smiling and talking nicely, they can detect that that's not a contingent interaction anymore," Saxe explains.

A few studies suggest that people with autism react differently. In 2006, **Sally Rogers** and colleagues from the University of California, Davis, conducted similar video experiments on 6-month-old babies.

Rogers found that when the live feed is swapped with a frozen image of the mother's face, most babies look immediately to the mother's eyes. In comparison, babies at high risk of being diagnosed with autism look much less at the eyes[8].

Saxe says she hopes her fMRI version of the experiment will pinpoint the neural differences in people with autism that correlate with these behavioral observations. After testing the paradigm on normal adults, she hopes to use it on teenagers with autism who have been treated using various behavioral interventions.

"We're hoping that if we get a measure on which pre-training autistic people differ from healthy people, then we'll be able to use that measure and ask if the training is making a difference," she says.

Saxe has also planned other autism-related experiments, including brain scans of people with autism making moral judgments, and a comprehensive survey of how specific brain regions develop in babies at risk of developing autism.

In the meantime, although she didn't have much luck with the judges, she is inspiring a new generation of scientists to thoroughly investigate the human experience. In one undergraduate course she designed last year, each student devoted the semester to carrying out a novel experiment in cognitive science.

"I can't have them do fake experiments," Saxe says. "The only reason to do science is because it's the only way to find out the answer, and you care what the answer is."

References:

1. Saxe R. and Kanwisher N. *Neuroimage* **19**, 1835-1842 (2003) **PubMed**
2. Saxe R. *et al. Neuropsychologia* **42**, 1435-1446 (2004) **PubMed**
3. Saxe R. *et al. Annu. Rev. Psychol.* **55**, 87-124 (2004) **PubMed**
4. Saxe R. *Trends Cogn. Sci.* **9**, 174-179 (2005) **PubMed**
5. Heberlein A.S. and Saxe R. *Neuroimage* **28**, 770-777 (2005) **PubMed**
6. Young L. and Saxe R. *J. Cogn. Neurosci.* (2008) Epub ahead of print **PubMed**
7. Bedny M *et al. J. Neurosci.* **28**, 11347-11353 (2008) **PubMed**
8. Merin N. *et al. J. Autism Dev. Disord.* **37**, 108-121 (2007) **PubMed**